REMARKS/ARGUMENTS

In response to the Office Action dated November 14, 2006, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of pending claims 12-26, and pass this application to allowance.

Applicants acknowledge the Examiner's withdrawal of the rejection of claims 12-26 under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 5,342,625 to Hauer et al., based on Applicants' previous response filed September 5, 2006.

In the office action of November 14, 2006, the Examiner has again rejected claims 12-26 under 35 U.S.C. §103(a) as allegedly obvious over the same Hauer et al reference, in view of U.S. Patent No. 5,962,019 to Cho et al. Applicants respectfully traverse this rejection.

Hauer et al. has been cited for teaching cyclosporin pharmaceutical compositions in the form of micro-emulsion pre-concentrates that are filled in hard gelatin capsules. The abstract, examples, and column 29, lines 11-14 are specifically cited for this teaching.

With respect to the abstract of Hauer et al., Applicants respectfully submit that the presently claimed invention is nowhere taught nor suggested. According to the abstract, the compositions of Hauer et al. typically comprise a C_{1-5} alkyl or tetrahydrofurfuryl di- or partial-ether of a low molecular weight mono- or poly-oxy-alkane diol, e.g., Transcutol or Glycofurol, as hydrophilic component. In contrast, the hydrophilic phase in the compositions of the present invention comprises a polyethylene glycol and at least one lower alkanol selected from ethanol and propylene glycol. According to the abstract of Hauer et al., the compositions also comprise a saccharide

monoester, e.g., raffinose or saccharose monolaurate. The presently claimed hard gelatin capsules of the present application comprise no such saccharide monoester.

At the top of page 5 of the office action, the Examiner refers to columns 26-29 of Hauer et al., directed to a cyclosporin formulation which include surfactants Cremophor RH40, which is described as a reaction product of hydrogenated or natural vegetable oil and ethylene glycol with an HLB value of 14-16. Therefore, the Examiner has taken the position that "the surfactant of Hauer meets the claimed surfactant component."

Applicants respectfully submit that in every example at columns 26-29 of Hauer et al., that employs Cremophor RH40, which according to the Examiner is a surfactant meeting Applicants' claims, the compositions also contain either Miglyol 812 or Myritol 318. *See e.g.,* compositions 1.2-3.11of Examples 1-3 of Hauer et al. Miglyol 812 is a fractionated coconut oil comprising caprylic-capric acid triglycerides. Myritol 318 also comprises caprylic-capric acid triglycerides. *See* column 9 of Hauer et al. These examples therefore, comprise oil *in addition* to (b) a surfactant of HLB value of at least 10, comprising a reaction product of hydrogenated or natural vegetable oil and ethylene glycol. Applicants further submit that the amounts of oils used in Examples 1-3 of Hauer et al. are not insignificant. *See e.g.* Example 3: Miglyol 812 at 16.6% by weight; Example 1, composition 1.5: Myritol 318 present at 100 mg/capsule out of a quantity of total components: 855.0 mg/capsule. In contrast, claims 12-26 of the present invention require that the composition be substantially free of any additional oil.

The Examiner has commented on page 5 of the office action, paragraph 1, final sentence, that "Not all of the compositions of Hauer contain additional oils and the claimed lower alkanols." Applicants submit that Examples 4-7 of Hauer et al. do not comprise additional oils. However, Examples 4-7 employ a C1-5 alkyl or tetrahydrofurfuryl di- or partial ether, e.g., (Transcutol or Glycofurol) which compounds are not required by the present claims. More importantly, the compositions in Examples

4-7 of Hauer et. al., do not contain a hydrophilic phase comprising a polyethylene glycol and at least one lower alkanol selected from ethanol and propylene glycol, as required by Applicants' claims 12-26.

Summarizing, in those instances in Hauer et al. where a surfactant of HLB value of at least 10 comprising a reaction product of natural or hydrogenated vegetable oil and ethylene glycol are present, and "therefore meet the claimed surfactant component" such compositions comprise additional oils. In contrast, the presently pending claims recite in addition to cyclosporin A, a surfactant and a hydrophilic phase, "the composition being substantially free of any additional oil." In other instances of Hauer et al. where additional oils may not be present, the compositions do not contain a hydrophilic phase comprising a polyethylene glycol and at least one lower alkanol selected from ethanol and propylene glycol, as required by Applicants' claims 12-26.

On page 5, line 12 of the office action, the Examiner readily admits that "Hauer fails to teach polyethylene glycol in combination with the lower alkanols." In order to fill the gap in teaching provided by Hauer et al., the Examiner has now added Cho et al. to the obviousness rejection.

Cho et al. has been cited for teaching hard gelatine capsules comprising cyclosporin formulations comprising at least one alkanol solvent constituting an alkanol having 2 to 3 carbon atoms and a co-solvent selected from fatty acids and diols, including polyethylene glycols. According to the Examiner, Cho et al. teach incorporating at least one surfactant, such as polyoxyalkylene surfactant having an HLB value of 5 to 20 or preferably 8 to 16. Applicants submit that Column 3, lines 62-63 of Cho et al. specifically teach "Also present in the orally acceptable vehicle will be at least one non-ionic polyoxyalkylene surfactant, usually not more than two non-ionic polyoxyalkylene surfactants." In contrast, the present claims recite a surfactant which comprises a reaction product of a natural or hydrogenated vegetable oil and ethylene glycol. There is

no motivation or suggestion in Cho et al., to substitute a surfactant comprising a reaction product of natural or hydrogenated vegetable oil and ethylene glycol of Applicants claims for the non-ionic polyoxyalkylene surfactant taught by Cho et al.

At page 6, lines 10-13 of the office action, the Examiner posits that the examples of Hauer do not necessarily contain oils. As discussed fully above, in every single example of Hauer et al., where a surfactant of HLB value of at least 10 comprising a reaction product of natural or hydrogenated vegetable oil and ethylene glycol are employed, the composition either contains additional oils (Examples 1-3) or else do not comprise a hydrophilic phase comprising a polyethylene glycol and at least one lower alkanol selected from ethanol and propylene glycol, wherein each lower alkanol present is present in an amount of less than 12% of the total weight of the composition disregarding the hard gelatine capsule, as required by Applicants' claims 12-26.

The Examiner has also taken the position that the instant specification does not define "substantially free of oils" or the upper limit that meets the limitation. In the first instance, Applicants respectfully submit that the claims recite "the composition being substantially free of any *additional* oil." Support for "substantially free of any additional oil" may be found throughout the specification, e.g., page 1, lines 28-29.

Generally, claim terms should be construed consistently with their ordinary and customary meanings, as determined by those of ordinary skill in the art. *Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.* 334 F.3d 1294, 1298, 67 USPQ2d 1132 (Fed. Cir. 2003). Absent an express intent to impart a novel meaning, claim terms take on their ordinary meaning. *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250, 48 USPQ2d 1117 (Fed. Cir. 1988).

Applicants respectfully submit therefore, that one skilled in the art, construing the phrase "the composition being substantially free of any *additional* oil" with its ordinary meaning, would understand there must be no substantial amount of oil in addition to the

components already recited. As fully discussed above, Hauer et al. in teaching compositions containing oils e.g., Miglyol 812, and Myritol 318, present in significant quantities in addition to a surfactant of HLB value of at least 10 comprising a reaction product of natural or hydrogenated vegetable oil and ethylene glycol, certainly do not suggest the presently claimed compositions, being substantially free of any additional oil. Cho et al. also do not suggest that a cyclosporine a formulation should be substantially free of any additional oil. Cho et al. instead describe the further addition of fatty acids or fatty acid esters. *See* Cho et al., column 4, lines 29-65.

Applicants respectfully submit that the Examiner has selected various bits and pieces of the compositions taught by Hauer et al., and Cho et al., and used such information to find the present claims obvious. In so doing, the Examiner has relied on the considerable benefit of hindsight reconstruction, which is never proper in making an obviousness determination. It is impermissible to first ascertain what an inventor did and then view the prior art in such a manner as to select random bits and pieces of art to reconstruct applicant's invention. *See In re Shuman*, 361 F.2d 1008, 1012, 150 USPQ 54,57 (CCPA 1966).

Further, the rejection of claimed subject matter under 35 U.S.C. §103(a) in view of a combination of prior art references requires that both the suggestion to carry out the claimed invention and reasonable expectation of success must be found in the prior art, *not in Applicant's disclosure. In re Vaeck*, 947 F.2d 488, 492, 20 USPQ2d 1438,1442 (Fed. Cir. 1991). Based on the foregoing, the specific combination of components of the hard gelatine capsules containing a pharmaceutical composition as presently claimed is not suggested by the combination of teachings provided by Hauer et al. in view of Cho et al.

Accordingly, in view of the foregoing comments, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 12-26 under 35 U.S.C. §103(a) and pass this application to issue.

Clams 12-26 have also been rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-9 of U.S. Patent No. 6,432,445 in view of U.S. Patent No. 5,962,019. Applicants respectfully traverse the rejection and submit that claims 12-26 of the present application do not define an invention that is merely an obvious variation of the invention claimed in the '445 patent. None of the claims of the '445 patent suggest a pharmaceutical composition comprising polyethylene glycol. The Examiner has cited the '019 patent apparently to show that any variation between claims 12-26 of the present application and the claims of the '445 patent (e.g., PEG recited in the present claims), would have been obvious to one of skill in the art. The Examiner has not, however, shown that one skilled in the art would find it obvious to limit the compositions to be substantially free of any additional oil. In fact, the '019 patent would suggest to one skilled in the art that additional oils may be used. See '019 patent, column 4, lines 42-65 where specific fatty acids for use in the compositions are enumerated. Thus, the presently pending claims do not recite obvious variants of the invention claimed in the '445 patent. Withdrawal of the nonstatutory obviousness-type double patenting rejection of claims 12-26 over claims 1-14 of U.S. Patent No. 6,767,445 in view of U.S. 5,962,019 is therefore warranted.

Claims12-26 have also been rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-14 of U.S. Patent No. 6,432,555 in view of U.S. Patent No. 5,962,019. Applicants respectfully traverse the rejection and submit that claims 12-26 of the present application do not define an invention that is merely an obvious variation of the invention claimed in the

'555 patent. None of the claims of the '555 patent would suggest to one skilled in the art that the compositions be substantially free of any additional oil. In fact, claims 2, and 5-7 of the '555 patent in reciting a lipophilic surfactant and a lipophilic component, require additional oil to that of the compositions of presently pending claims 12-26. Further, the '019 patent at column 4, lines 42-65, would suggest to one skilled in the art that additional oils may be used. Thus, the presently pending claims do not recite obvious variants of the invention claimed in the '555 patent. Withdrawal of the nonstatutory obviousness-type double patenting rejection of claims 12-26 over claims 1-14 of U.S. Patent No. 6,767,555 in view of U.S. 5,962,019 is therefore also warranted.

In view of the foregoing remarks and amendments, it is firmly believed that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

Novartis
Corporate Intellectual Property
One Health Plaza, Building 430
East Hanover, NJ 07936-1080
(862) 778-2614

Ann R. Pokalsky
Attorney for Applicants
Reg. No. 34,697